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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
TURNER, SHARON L

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 08/12/2002 29

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/183,972	Hageman
Examiner	**Art Unit**
Sharon L. Turner, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 5-20-02

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1, 2, 4-13, 23-27, and 31-55 is/are pending in the applica

4a) Of the above, claim(s) 1, 4-13, 23-27, and 31-45 is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 2 and 46-55 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims 1, 2, 4-13, 23-27, and 31-55 are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Request for Reconsideration

1. The amendment filed 5-20-02 has been entered into the record and has been fully considered.

2. Claims 1-2, 4-13, 23-27, and 31-55 are pending.

Election/Restriction

3. Claims 1, 4-13, 23-27, and 31-45 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 15 and 25.

4. It is noted that the status of the claims as indicated above differs from that of Applicant's Remarks. There is no record of cancellation of claims 1, 4-13, 23-27, 31-32 and 33-45. Claims 2 and 46-55 are under consideration.

5. This application contains claims 1, 4-13, 23-27, 31-32 and 33-45 drawn to an invention nonelected with traverse in Paper No. 15 and 25. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Rejections

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 2 and 46-55 stand rejected as set forth in Paper No's 17 (10-25-00), 20 (5-15-01), and 26(1-30-02) under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

Applicants argue that the disclosure provides specific utilities for the claimed sequences, that all evidence indicates practical utilities of the IPM sequences, that the disclosed utilities are specific, not general and that specific utility does not mean exact or unique biochemical/physiological function. Applicants additionally argue that real-world utilities exist that would have been readily apparent.

With respect to evidence of practical utility for the claimed IPM sequences, applicants argue that the prior art and disclosure suggest IPM sequences are involved in retinal adhesion and ocular disorders based on expression in retinal tissue as shown in Felbor et al., Cytogene. Cell Genet. 81:12-17, 1998 at p. 16, left column. Applicants also note the teachings of p. 20, lines 28-30 and p. 21, lines 39 that IPM150 contain hyaluronan-binding motifs and EGF-like domains and thus conclude that IPM150 could interact with hyaluronan or promote survival of neighboring cells based on the fact that EGF-like domains are present in many extracellular matrix proteins which promote survival of neighboring cells. Applicants assert that the IPM sequences are genetically linked to a number of macular dystrophies noting the teachings of Felbor and the similar chromosomal mapping locales (6q13-q15 for IPMG1 in comparison to 6q14.2-q15 for

IPM150). Based on the disclosure and Felbor's teachings applicants conclude that there is no doubt that the invention can have practical and useful applications for example in diagnosing by detecting mutations or abnormal expression of the IPM molecules and treating via gene therapy in ocular disorders associated with abnormal retinal adhesion such as retinal detachment and macular degeneration.

With respect to specificity, applicants argue that the disclosed utilities are not general in that their expression in retinal tissue and genetic linkage to certain specific ocular diseases is disclosed. Applicants assert that Felbor believes the IPM150 locus to be a candidate locus for retinopathies and thus that Felbor evidences specificity to the instantly claimed sequences.

With respect to exact or unique biochemical/physiological function applicants argue that MPEP21.07.03, I provides that only a reasonable correlation between a disclosed biological activity (e.g., expression in retinal tissue and hyaluronan-binding) and a disease state (e.g., retinopathies) is required. Thus, applicants conclude that the specification provides sufficient utility for IPM150 sequences claimed.

Applicants further argue that the real-world utility of screening via polynucleotide array technology would have been readily apparent to the claimed sequences from the disclosure.

Applicants arguments filed 5-20-02 have been fully considered but are not persuasive. In response to Applicants referral to the Felbor reference for its teachings, it is noted that the publication discloses the expression, genomic organization and chromosome location of a novel interphotorecetor matrix gene IPMG1 and not of instant SEQ ID NO: 1, 3 or 5 as claimed. In

fact SEQ ID NO's:1, 3 and 5 differ substantially, see in particular attached alignment which shows merely 15.3 % similarity to SEQ ID NO:1, 25% similarity for SEQ ID NO:3 and less than .5% similarity to SEQ ID NO:5. Moreover, the reference teaches nothing of the expression, genomic organization or chromosomal localization of the instantly claimed molecules.

Applicants disclosure at p. 8, line 16-p. 9, line 3 teach expression of IMP150 in neural retinae, specifically in rod and cone photoreceptor cells and that the gene is located on chromosome 6q14.2-q15. However, the disclosure fails to note the significance of such data to specific disease, diagnosis or treatment as previously set forth in the Action of Paper No. 26. Furthermore, while predicted hyaluronan binding motifs and EGF-like domains are noted in the IPM150 sequence, the significance of such domains are not established but are merely presumed. There is no demonstration of IPM150-hyaluronan binding, IPM150 interaction with hyaluronan or the promotion of survival of any cell type by IPM150 within the retinae, rod, cone or eye in general. Moreover, neither Felbor nor the disclosure establishes that the IPM150 sequences of SEQ ID Nos: 1, 3, and 5 are genetically linked to any particular macular dystrophy. Such presumption can be merely be based on the proximity of a gene to a chromosomal location which is hypothesized to contribute to the noted abnormalities. Such presumption is not factually based nor accepted in the art. As evidence, even Felbor acknowledges that such proximity is not definitive but merely, "a candidate gene for retinal dystrophies," see in particular p. 16, column 2, last paragraph. Although, "an attractive basis for further mutational analysis," Felbor does not suggest or teach a linkage between the IPMG1 gene and any retinal disease, diagnosis or suitable

treatment. Similarly the lack of such data highlights the deficiencies in the instant application in that the data presented for the IPM150 sequence is not disclosed as being genetically linked, associated with or capable of providing for any diagnostic, prognostic or therapeutic treatment relative to retinopathies in general or to macular degeneration as suggested by applicants. Further, there is no basis for concluding particular function based upon the identification of hyaluronan binding motifs or EGF-like domains as previously noted in Przysiecki et al., of record. In further support, the skilled artisan readily recognizes an unpredictability in the art in the determination of protein function based upon divergent and even conserved structure, see in particular Skolnick et al., Trends in Biotech., 18(1):34-39, 2000. Thus, there is doubt that the present invention has practical and useful applications, as none are disclosed. With respect to applicants conclusion that applications in diagnosis or treatment could be found via detection of a mutation, abnormal expression or gene therapy, the statement highlights the lack of a defined specific and substantial utility for the invention as no specific gene mutation, abnormal expression or form of gene therapy has been shown to be of diagnostic, prognostic or therapeutic effect. Moreover, it is emphasized that the artisan is still not apprised of how to make and or use any such method, assay, or treatment whereby diagnostic, prognostic or therapeutic effect is achieved. In particular the specific mutations, steps of analyzing or identifying such mutations, diseases associated with such mutations or methods of overcoming the detrimental effects of such mutations are not disclosed. At most the specification arrives at a strong suggestion for further research to discover such potential uses.

In response to Applicant's specificity arguments it is noted that the claimed sequences are not established as being genetically linked to certain specific ocular diseases and that expression in retinal tissue alone fails to disclose a particular use or significance to the claimed sequences. The above discussion notes that no linkage analysis has been performed for any disease to establish a genetic link to either IPMG1 of the prior art or IPM150 of instant claims. Applicants assert that Felbor believes the IPM150 locus to be a candidate locus for retinopathies and thus that Felbor evidences specificity to the instantly claimed sequences. However, it is again noted that Felbor expresses an unsubstantiated hypothesis and that the sequences of IMPG1 although near in chromosomal location are not established as having the same localization on the chromosome, nor are the sequences the same as those claimed represented by SEQ ID NO:1, 3 or 5. Thus, the recitation does appear to be general in that the sequences are merely hypothesized to be somehow relevant either in diagnosis or therapy of a retinopathy or ocular disease. Thus, the utilities do not appear to be either specific, substantial or well-established.

In response to applicants arguments that only a reasonable correlation between a disclosed biological activity and disease state is required, it is noted that MPEP 2107.03, I., states that;

> As a general matter, evidence of pharmacological or other biological activity of a compound will be relevant to an asserted therapeutic use if there is a reasonable correlation between the activity in question and the asserted utility. Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); Nelson v. Bowler, 626 F.2d 853, 206 USPQ 881 (CCPA 1980). An applicant can establish this reasonable correlation by relying on statistically relevant data documenting the activity of a compound or

> composition, arguments or reasoning, documentary evidence (e.g., articles in scientific journals), or any combination thereof. The applicant does not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating humans where such a utility is asserted. Instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the activity and the asserted use. Nelson v. Bowler, 626 F.2d 853, 857, 206 USPQ 881, 884 (CCPA 1980).

However, in instant case there is no correlation established between retinopathies and retinal expression or hyaluronan binding. As evidence, note applicants discussion at p. 3-8 of the specification. Therein it is noted that a number of peptides may be expressed within the retina, including cone matrix sheaths, and IPM, "proteins, glycoproteins and proteoglycans," which are all expressed in the retinae, see p. 3 but yet which are not known to specifically relate to disease or disease states. As noted at p. 5, "relatively little is known, however, about the molecular nature, origin, or precise functions of most IPM molecules". The specification does not teach such a correlation for IPM150 as claimed. While the specification at p. 6, lines 18-26 does disclose for example the correlation of loss of chondroitin 6 sulfate to mucopolysaccharidosis and cone outer segment loss, the specification does not teach a correlation to retinal protein expression in general, or to hyaluronan binding in ocular disease or to a broad class of diseases recognized as retinopathies. Thus, there is no reasonable correlation of a biological molecule or molecular function associated with the IPM150 molecule which is associated with retinopathies in general or any specific diagnostic, prognostic or therapeutic assay or effect as disclosed utilizing SEQ ID Nos:1, 3 and 5 as claimed. Further in support of a lack of such correlation is

the summarized statements at p. 7, lines 23-27, "identification of novel IPM components and their genes will make possible novel therapeutic and diagnostic agents for diseases or conditions associated with abnormal interphotoreceptor matrix (IPM), such as retinal detachment, chorioretinal degenerations, retinal degenerations and macular degenerations such as AMD, or other dystrophies or degenerations involving IPM, cones or rods." At most the disclosure establishes that the IPM150 molecule is expressed in retinae, but the specification fails to disclose any correlation of IPM150 expression or mutation with any particular retinal disorder, prognostic, diagnostic or therapeutic as implied by Applicant's arguments. Thus, the specification does not provide a reasonable correlation or structure/function correlation for the claimed molecules such that the artisan could preclude how to use the nucleic acids for diagnostic, prognostic or therapeutic purposes. The specific assays, requirements and outcomes are not disclosed and thus the artisan is not readily provided with the significance of the IPM150 molecules as claimed. There is no disclosed utility, a method for making it and method of using it which fulfills the requirements of 35 USC 101 and 35 USC 112 as implied by applicants.

In response to applicants asserted established use in polynucleotide array technology, it is noted that such screening methods are not specific to the IPM150 sequence but instead rely upon the broad general class of molecules known as polynucleotides. Any polynucleotide could similarly be used for screening and in particular any ocularly expressed polynucleotide could be used for screening. However, the use of the IPM150 molecule in such screens fails to provide beneficial results until the significance of its inclusion is established. For example, is the

expression level predictably correlated to a disease state. In instant case no particular significance of the IPM150 molecule in such screening is disclosed and thus the molecule appears to merely provide a research reagent for further undue experimentation such that the real-world context of use or significance can be established. The inclusion of the molecule for the sole purpose of further research fails to delineate a context of use which is specific or substantial to the molecule. The fact that a general research method is well established fails to provide significance for any general class of molecules which could be used as a matter of its inclusion in the broad general class of chemical compounds, see in particular *Brenner v. Manson.* Thus, the use of the IPM150 sequence in polynucleotide array screening assays does not arise to the provision of utility as required by 35 USC 101.

Claims 2 and 46-55 stand rejected as set forth in Paper No's 17 (10-25-00), 20 (5-15-01), and 26 (1-30-02) under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Status of Claims

8. No claims are allowed.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (703) 308-4623.

Gary L. Kunz

GARY L. KUNZ
SUPERVISORY PATENT EXAMINER
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Sharon L. Turner, Ph.D.
August 6, 2002